PATENT
Docket No. 204372000320

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on November 4, 1996.

Nancy J. Robins

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Lynn E. Spitler et al.

Serial No.: 08/288,057

Filing Date: 10 August 1994

For: PROSTATIC CANCER VACCINE

Examiner: P. Gambel

Group Art Unit: 1816

DECLARATION OF ROBERT OLDHAM, MD PURSUANT TO 37 C.F.R § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Robert Oldham, MD, declare as follows:

1. I am the Director of the Biological Therapy Institute in Franklin, Tennessee. A copy of my *Curriculum Vitae* is attached hereto as Exhibit A. I am a consultant to Jenner Technologies, the assignee of the present application.

2. I have reviewed the Declaration Under 37 C.F.R. 1.132 prepared by Dr. Lynn E. Spitler describing the results of a clinical study directed to the use of prostate specific antigen (PSA) as an active ingredient in an antiprostate cancer vaccine. I am also familiar with the study itself, and with the results that were obtained.

3. The purpose of the study was to obtain evidence that the vaccines would raise a sufficient cellular immune response to have a beneficial effect with respect to prostate tumors. Such a result could be shown directly by measuring cytotoxic lymphocyte (CTL) generation; however, I am aware that this was not possible in these studies because the assay was not satisfactory because of the lack of an appropriate target cell for the assay.

4. The responses measured are understood in the art to be satisfactory substitutes for measuring CTLs. Thus, the proliferation of lymphocytes from two of the patients in response to contact with PSA or in response to peptides representing putative PSA epitopes is indicative of an appropriate cellular immune response. The ability of PSA or PSA derived peptides to stimulate cytokine production -- i.e., gamma interferon and IL-4 production -- from lymphocytes in these patients also indicates that the cellular response is obtained specifically with respect to PSA. The observation of the development of a positive skin test response to PSA in one patient is also consistent with these observations showing the development of cell-mediated immunity in the patients.

5. In my opinion, the results obtained in this clinical study provide evidence that the vaccines are likely to be effective in exerting a beneficial effect on patients with prostate tumors or at risk for prostate tumors.

6. The efficacy shown for the vaccine tested in the foregoing clinical studies further provides evidence that analogous vaccines based on host tissue antigen, such as prostate specific membrane antigen (PSMA) and prostate acid phosphatase (PAP) would behave in a similar manner. It is also well known that if the entire antigen is effective as a vaccine, portions of the antigen will be effective as well, especially if manipulated by art-known methods to enhance their immunogenicity, such as by coupling them to carrier.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

October 10, 1996

Robert Oldham, MD

Revised: 10/1/95

CURRICULUM VITA

Name	Robert K. Oldham, M.D
Permanent Address	357 Riverside Drive Franklin, Tennessee 37064 615/791-4073
Social Security #:	500-40-8139
Date/Place of Birth:	9/16/41; Pocatello, Idaho
Marital Status:	Single (5 sons)
College:	University of Missouri, Columbia, MO Chemical Engineering Pre-Medical Sciences
Medical School:	1968, Medical Degree University of Missouri Columbia, Missouri
Graduate Training:	1970-1971 Immunology NIH Graduate Program

Professional Employment

1991 - Present	Chairman of the Board and President Cancer Therapeutics Inc. 357 Riverside Drive Franklin, Tennessee 37064
1992 - Present	Chairman of the Board and President American Patient Services 357 Riverside Drive Franklin, Tennessee 37064
1986 - Present	Chairman of the Board Media America 357 Riverside Drive Franklin, Tennessee 37064

Consultant:

1984 - 1986	Wellcome Biotechnology Ltd. Kent, England
1989 - Present	Amersham International Buckinghamshire, England
1991 - Present	Cancer Treatment Centers of America Zion, Illinois
1994 - Present	Applied Immune Sciences Santa Clara, California 95054

Editorial Boards:

1992 - Present	Cancer Biotherapy, Founder, (now Cancer Biotherapy & Radiopharmaceuticals) Editor-in-Chief
1990 - Present	In Vivo, Editorial Board Natural Immunity and Cell Growth Regulation, Editorial Board
1988 - 1992	Molecular Biotherapy, Founder and Editor-in-Chief
1982 - 1989	Journal of Biological Response Modifiers (now Journal of Immunotherapy) Founder and Editor-in-Chief
1982 - 1985	Cancer Immunology and Immunotherapy, Editorial Board

Major Research Interests:

Cancer Biotherapy
Biologicals and Biological Response Modifiers
Investigative Trials in Clinical Oncology
Cellular Therapy of Cancer
Monoclonal Antibodies & Immunoconjugates in Cancer Treatment
In Vitro Assays in Tumor Immunology
Privatization of Cancer Research

Professional Employment (Continued)

1984 - Present	Founder and Director Biological Therapy Institute 357 Riverside Drive Franklin, Tennessee 37064
1984 - Present	Clinical Professor of Medicine Hematology/Oncology University of Missouri Columbia, Missouri 65212
1984 - 1990	Founder, Scientific Director and Chairman of the Board Biotherapeutics Inc. (Now Response Technologies, Inc. Technologies, Inc.) Memphis, Tennessee 38117
1984 - 1986	Founder and Consultant Biomedical Research Center University of British Columbia Vancouver, British Columbia V6T 2B5
1980 - 1984	Founding Director, Biological Response Modifiers Program Associate Director, Division of Cancer Treatment National Cancer Institute Frederick, Maryland 21701
1975 - 1980	Founder and Director, Div. of Oncology Associate Professor of Medicine Associate Director; Cancer Center Vanderbilt University Medical Center Nashville, Tennessee 37232

Professional Employment Continued.

1974 - 1975	Senior Investigator Laboratory of Immunodiagnosis National Cancer Institute Bethesda, Maryland 20205
1973 - 1974	Senior Investigator Cellular and Tumor Immunology Section Laboratory of Cell Biology National Cancer Institute Bethesda, Maryland 20205
1972 - 1973	Research Associate with Professor G. Mathe ICIG - Hospital Paul Brousse Villejuif, France
1971 - 1972	Clinical Associate, Cellular and Tumor Immunology Section Laboratory of Cell Biology National Cancer Institute Bethesda, Maryland 20205
1970 - 1971	Clinical Associate, Radiation Branch National Cancer Institute Bethesda, Maryland 20205
1968 - 1970	Internal Medicine Intern and Resident Vanderbilt University Hospital Nashville, Tennessee 37205

Clinical Group Appointments:

1976 - 1980	Principal Investigator - Vanderbilt Southeastern Oncology Study Group (NCI)
1978 - 1980	Principal Investigator - Vanderbilt Lung Cancer Study Group (NCI)
1986 - 1990	Founder and Group Chairman - National Biotherapy Study Group
1986-Present	Principal Investigator - Biological Therapy Institute - National Biotherapy Study Group

Fellowship Experience:

1970 - 1972	Medical Oncology Fellowship, National Cancer Institute - Bethesda, Maryland
1967	PHS Cancer Clinical Fellowship, Lemuel Shattuck Hospital-Jamaica Plain - Boston, Massachusetts
1967	PHS Cancer Clinical Fellowship, Ellis Fischel Cancer Hospital - Columbia, Missouri
1965	PHS Student Research Fellowship, University of Missouri Medical School - Columbia, Missouri

Honors, Awards and Societies:

1967	Alpha Omega Alpha
1970	Diplomat, National Board of Medical Examiners
1975	Diplomat, American Board of Internal Medicine
1975	Diplomat, Medical Oncology, American Board of Internal Medicine
1976	American Association of Immunologists
1976	International Society for Experimental Hematology
1976	Williamson County Medical Society
1977	Southern Medical Association
1977	American Federation for Clinical Research
1977	American Society for Clinical Oncology
1978	American College of Physicians, Fellow
1979	Southern Society for Clinical Investigation
1982	American Osler Society
1984	Society for Biological Therapy, Founder President - May 1984 to November 1986
1984	Reticuloendothelial Society
1986	National Biotherapy Study Group, Founder Group Chairman - 1986 to 1990
1990	Association of Community Cancer Centers
1994	International Cytokine Society
1994	The American Association of Bioethics

Licensure:

Tennessee, Maryland and Missouri

Major Accomplishments (Curriculum Vitae #)

Discovery of Natural Killer Cells
(#8, 9, 27, 28, 31, 46, 47, 56, 90, 92, 121, 157 323)

Development of improved therapy for small cell lung cancer
(#66, 69, 78, 80, 85, 95, 103, 105, 108, 124, 177)

Development of improved therapy for ovarian cancer
(#99, 102, 125)

Development of improved methods in detecting and treating extragonadal germ cell tumors and other poorly differentiated tumors
(#22, 87, 93, 122, 123, 227, 228; 5-Book)

Use of cryopreserved cells for standardized immunological testing
(#37, 38, 40, 41, 45, 49, 52, 120)

Cancer Biotherapy: first to use the term to describe a fourth modality of cancer treatment
(#109, 114, 119, 128, 129, 134, 137, 139, 141, 146, 151 153, 154, 161, 169, 173, 174, 175, 176, 179, 181, 183,184, 188, 193, 197, 204, 206, 212, 225, 240, 249, 250,184, 188, 193, 197, 204, 206, 212, 225, 240, 249, 250,252, 260, 261, 262, 264, 265, 266, 267, 301, 302, 314,319, 322, 324, 325, 332, 333, 338, 339, 340, 343, 344, 346, 349, 356, 357, 358, 360, 361, 362, 363)10 Books)

Monoclonal antibodies and immunoconjugates in cancer treatment: Did groundbreaking experiments with toxin, drug and isotope conjugates
(#125, 126, 140, 143, 144, 145, 150, 152, 155, 156, 159, 160, 165, 180, 181, 182, 185, 187, 195, 196, 198, 199, 206, 218, 223, 224, 235, 238, 241, 244, 246, 247, 248, 251, 253, 254, 263, 278, 279, 285, 286, 287, 288, 291, 306, 307, 310, 311, 318, 325, 327, 342, 347)

Cytokine and Cellular Therapy: Conducted some of initial clinical experiments with IL-2 in LAK and T cell therapy
(#249, 255, 259, 281, 290, 294, 295, 298, 301, 302, 309, 311, 314, 322,324,332,333,349,356,357, 358, 361, 362)

Individualized Cancer Treatment: Conducted specific laboratory and clinical experiments demonstrating that each cancer in each patient has unique characteristics which may require unique, individualized treatment
(#267, 279, 285- 288, 291, 306, 307, 310, 318, 325, 327, 342, 347)

Privatization of Cancer Research: Brought attention to clinical research opportunities in the private sector. Published widely on problems of access to new technologies and the funding of clinical research
(#134, 205, 206, 207, 231, 236, 245, 256, 257, 268, 269,282, 284, 289, 293, 308, 312, 316, 317, 319, 321, 325, 326, 330, 331, 334, 335, 350, 352, 353, 354, 355, 358,359, 364, 11-Books)

Publications

Over 380 papers published in the medical/scientific literature

Thousands of abstracts, posters and presentations at various meetings on cancer research and treatment

Editor of Principles of Cancer Biotherapy, the first comprehensive textbook on the fourth modality of cancer treatment (Now in Third Edition).

Founding Editor of Cancer Biotherapy, (now Cancer Biotherapy & Radiopharmaceuticals), Molecular Biotherapy and the Journal of Biological Response Modifiers (now Journal of Immunotherapy).

Author or editor of thirteen books on cancer research and treatment

BIBLIOGRAPHY

Published Papers

1 Oldham, R K Terminal cancer - A patient oriented approach J Tenn Med Assoc , 63 206, 1970

2 Oldham, R K Aseptic meningitis following the intrathecal injection of RISA Radiology, 97 317, 1970

3 Oldham, R K Eosinophilic Granuloma South Med J , 64 978, 1971

4 Oldham, R K and Pomeroy, T C Vincristine induced inappropriate ADH syndrome South Med J , 65 1010-1012, 1972

5 Oldham, R K and Pomeroy, T C Treatment of Ewing's sarcoma with Adriamycin Cancer Chemotherapy Reports, 56 635-639, 1972

6 Oldham, R K and Pomeroy, T C Extramedullary plasmacytomas following successful radiotherapy of Hodgkin's disease Clinical and immunological aspects American J. Med , 54 761-767, 1973

7 Oldham, R K , Larson, S M., and Givelber, H M , Chretien, P B , and Johnson, R E A preliminary study of 51Cr-labeled platelets for evaluation of splenic sequestration in chronic lymphcytic leukemia J Nuclear Med , 37,219-222, 1973

8 Oldham, R K , Siwarski, D , McCoy, J L , Plata, E J , and Herberman, R B Evaluation of a cell-mediated cytotoxicity assay utilizing 125Iododeoxyuridine labeled tissued culture targets Nat Cancer Inst Monongr , 37 49-58, 1973

9 Oldham, R K., Herberman, R B Evalution of cell-mediated cytotoxic reactivity against tumor associate antigen utilizing 125Iododeoxyuridine labeled target cells J Immunol , 111 1862-1971, 1973

10 Lemevel, B P , Oldham, R K , Wells, S A , and Herberman, R B An evaluation of 125Iododeoxyuridine as a cellular label for in vitro assays - Kinetics of incorporation and toxicity J Nat Cancer Inst , 51 1511-1558, 1973

11 Oldham, R K and Simmler, M C The use of cryopreserved lymphocytes and lymphoblasts in 51Cr lymphocyte cytotoxicity In Weiner, R S , Oldham, R K , and Schwarzenberg, L (Eds) The Cryopreservation of Normal and Neoplastic Cells, Inserm, Institute National de la Sante et de la Recherche Medicale Paris, pp 161 169, 1973

12 Oldham, R K and Simmler, M C Possible role of lymphocyte cytotoxicity in bone marrow grafting Trans. Proceed., 6 417, 1974

13 Jasmin, C , Bricout, F , Huraux, J M , Weiner, R., Oldham, R K., and Mathe, G. A study of viral infections in patients treated with a combination of 6 meraptopurine-methotrexate Preliminary results In Mathe, G., and Oldham, R K (Eds) Recent Results in Cancer Research Complications of Cancer Chemotherapy, Vol 49 New York, Springer-Verlag, pp 29-33, 1974

14 Mathe, G. and Oldham, R.K. Introduction In Mathe, G. and Oldham, R.K. (Eds.): Complications of Cancer Chemotherapy. New York, Springer-Verlag, pp. 1-2, 1974

15 Beard, J., Weiner, R.S., Oldham, R.K., and Mathe, G.: Immune responsiveness in acute lymphocytic leukemia patients under chemotherapy and immunotherapy. A preliminary report In Mathe, G. and Oldham, R.K. (Eds.): Recent Results in Cancer Research: Complications of Cancer Chemotherapy. New York, Springer-Verlag, pp. 56-60, 1974

16 Belpomme, D., Carde, P., Oldham, R.K., Mathe, G., Jacquillat, N., Chelloul, N., Weil, M., Auclerc, C., Weisgerber, G., Tanzer, T., and Bernard, J. Malignancies possibly secondary to anticancer therapy In Mathe, G., and Oldham, R.K. (Eds.) Recent Results in Cancer Research: Complications of Cancer Chemotherapy. New York, Springer-Verlag, pp. 115-123, 1974.

17 Mathe, G., Schwarzenberg, L., Pouillart, P., Weiner, R., Oldham, R.K., Jasmin, C., Hayat, M., Schneider, M., Amiel, J.L., Ceoara, B., and Steresco-Musset, M. Essae de Traitement de divers hematosarcomas par le 4-demethyl-epipodophyllotoxine beta.D. thenylidene glucoside(VM 26 ou EPT) La Nouvelle Presse Med., 3:337-451, 1974

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42 Campbell, D.A., Manders, E.K., Oehler, J.R., Bonnard, G.D., Oldham, R.K., Herberman, R.B. Inhibition of in vitro lymphoproliferative response by in vivo passaged rat 13762 mammary adenocarcinoma cells, I: Characteristics of inhibition and evidence for an infectious agent. Cell. Immunol., 33:363-377, 1977.

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46 Oldham, R.K., Ortaldo, J., Herberman, R.B.: Natural cytotoxic reactivity of rat lymphocytes as measured by the (125I) iododeoxyuridine and tritiated proline microcytotoxicity assays in the Gross virus induced lymphoma system Cancer Res 32 4457-4463, 1977.

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